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Letter to the Editor

Lamin A/C gene (*LMNA*) mutation associated with laminopathy: A rare cause of idiopathic acro-osteolysis

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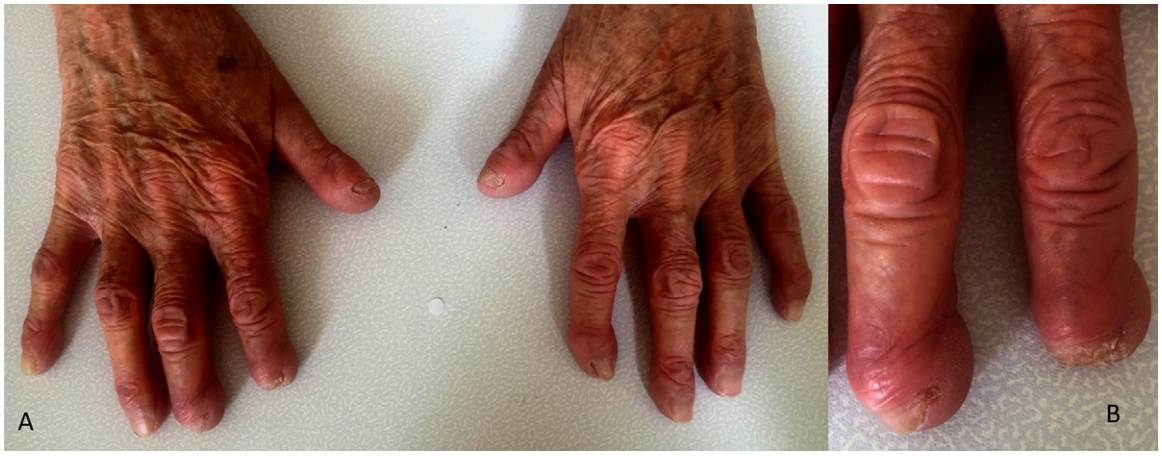

Fig. 1. A. Photograph of both hands showing thin fingers, with pseudo-clubbing and a shortening of the first three fingers on right hand and the first left finger. B. Photograph of the second and third right fingers with shortening of the last phalanx.

Acro-osteolysis (AO) is a term describing the distal lysis of finger and toe phalanges. AO is most often acquired [1]. The genetic or syndromic forms of AO are rarer, the best known being Hajdu-Cheney syndrome [2,3].

We report a case of a rare idiopathic form of acro-osteolysis attributed to a mutation of the lamin A/C (*LMNA*) gene associated with laminopathies.

A 63-year-old woman came in for consultation at the rheumatology department for advice concerning fingertip pain, associated with digital deformities, which had been progressing for 10 years. She also had high blood pressure and heart rhythm disorders (atrial fibrillation and atrioventricular block) which required a pace-maker. The patient's daughter had painful fingers, and her son had heart disease.

Clinically, she had shortened fingers, predominantly at the first three rays, which appeared very thin with pseudo-clubbing and brachyonychia (Fig. 1), a facial dysmorphism with significant malar hypoplasia, an extensive diffuse cutaneous xerosis and flaky skin.

X-rays showed longitudinal AO of several fingers of both hands (Fig. 2).

There were no abnormalities of blood count, parameters of inflammation, liver function or renal function. Hepatitis and syphilis serologies were negative. The phospho-calcium balance and serum uricaemia were normal. The immunological assessment was negative, and no anomalies were found on the thoraco-abdomino-pelvic CT scan, trans-thoracic echocardiography, capillaroscopy or dual X-ray absorptiometry (DXA). The electromyogram was considered normal, with no arguments for myopathy.

An acquired form of AO was excluded. The association of an idiopathic longitudinal AO with various clinical and paraclinal elements and the existence of family history made us suspect a laminopathy. The diagnosis was confirmed after genetic testing, finding a heterozygous mutation of the *LMNA* gene, c.1003 C > T (p.Arg335Trp or p.R335 W) localized in exon 6 of this gene (NM_170707.3).

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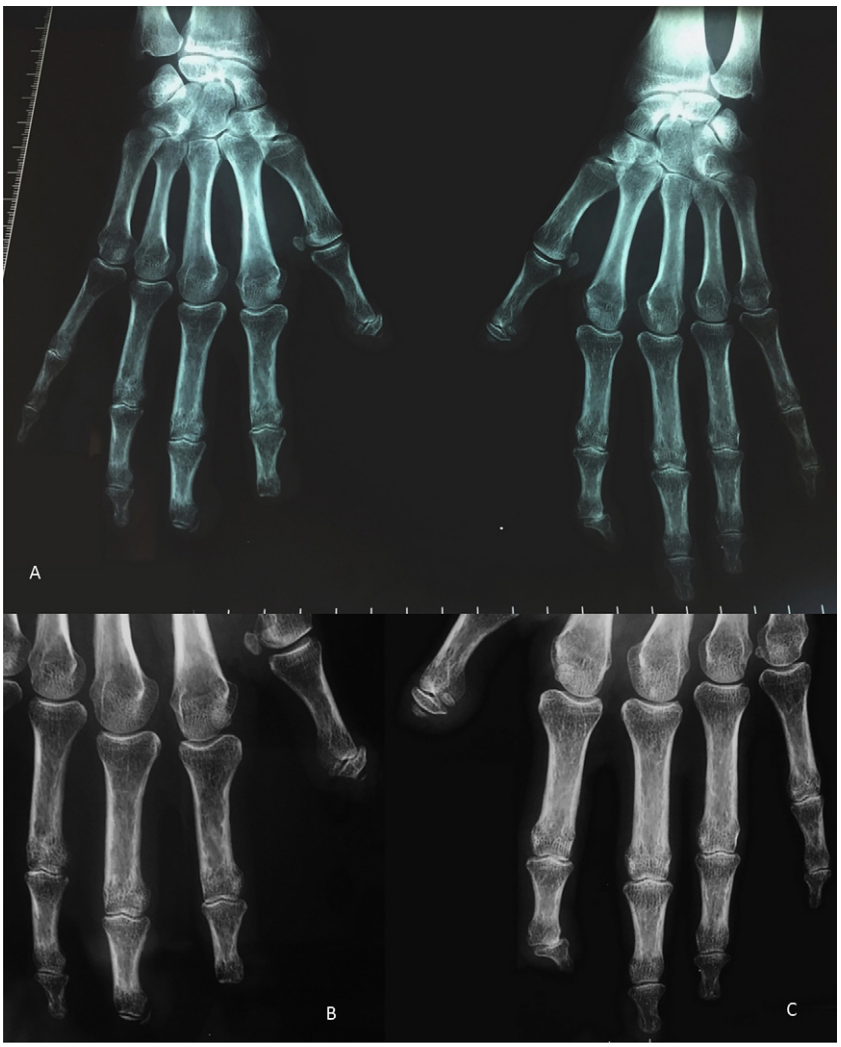

Fig. 2. A. X-ray of both hands; B. X-ray enlargement of the right hand; C. X-ray enlargement of the left hand; Evidence of distal phalanx resorption predominating in the first three right fingers and the first left finger in favour of longitudinal acro-osteolysis.

Laminopathies are rare diseases linked to mutations in the lamin A/C (*LMNA*) gene (1q22) encoding lamins A and C, proteins involved in the structure and function of the cell nucleus and present in all differentiated tissues [4]. Their phenotypes are variable, associating various cardinal signs such as AO, lipodystrophy, myopathy, premature ageing, and cardiac conduction disorders, which are frequently described [4]. The set of phenotypic manifestations is mutation-dependent in most cases and there is currently no specific curative treatment. These diseases are predominantly autosomal dominant, but autosomal recessive inheritance is also described. AO has already been described in some laminopathies, most often in genetic studies interested in acro-mandibular dysplasia [5,6]. It is interesting to note that, in our patient, AO was progressive and characterized by a late onset. Several types of mutations in the *LMNA* gene have been reported [7]. The mutation presented by our patient is of the missense type and has already been described in a subject with a cardiopathy associated with acro-osteolysis and hypertriglyceridemia [8], and in two familial cases, in patients with dilated cardiac disease with conductive disorders [9]. A laminopathy is a very rare pathology that rheumatologists may suspect in patients with primitive AO, combined with family history and multi-systemic (cardiac, cutaneous or muscular) involvement.

Disclosure of interest

The authors declare that they have no competing interest.

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